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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/227,742 01/08/99 BLOOM

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EXAMINER

HM12/0412

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RAILEY, J

ART UNIT

PAPER NUMBER

1636

DATE MAILED:

04/12/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/227,742

Applicant(s)

Bloom et al.

Examiner

J. Railey

Group Art Unit

1636



☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-44 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-44 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-44 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 5,891,692. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claimed methods of obtaining a bacterium having enhanced viability or transformation efficiency, as well as the methods for obtaining such bacteria are essentially the same invention as the methods claimed for making such bacteria in the issued patent.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-14 and 29-44 are rejected under 35 U.S.C. 102(b) as being anticipated by either

of Ulrich et al. [J. Bact. **154**(1):221-230 (1983)] or de Mendoza et al. [J. Biol. Chem. **258**(4):2098-2101 (1983)].

Applicant claims bacteria which have altered fatty acid content and hence have enhanced transformation efficiency or enhanced viability at low temperature storage as a result. These bacteria isolates may be generated by transforming with a gene involved in changing the unsaturated fatty acid content of the membrane to generate the phenotype claimed. Also claimed are methods of obtaining such bacteria by introducing a gene involved in changing the fatty acid content of the bacterium

Either of Ulrich et al. or de Mendoza et al. teach transformation of *E. coli* with the *fabB* gene which encodes β -ketoacyl-carrier protein (ACP). See Ulrich Figure 2, transformants with plasmid pDM4 or pDM2. See all of de Mendoza et al. These transformants alter the fatty acid composition of the cell membrane and therefore have all of the properties inherent as claimed by applicant. Applicant's claimed method of making the bacteria as well as the bacteria produced are indistinguishable from those of the prior art. Discovery of new property or use of previously known composition, even if unobvious from prior art, cannot impart patentability to claims to known composition. *In re Spada* 15 USPQ2d 1655 (CAFC, 1990). Likewise, applicant's method claims are essentially those of the prior art for transformation of the bacteria. The preamble to the claim which describes inherent properties of the modified bacteria do not distinguish applicant's claimed method.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for enhancing the viability of bacteria during low temperature storage or for enhancing transformation efficiency following low temperature storage by transforming bacteria with genes which increase the percent of unsaturated fatty acids in the cell membrane, does not reasonably provide enablement for other modifications of the bacteria which would result in the properties as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification teaches at page 13 beginning at the last paragraph that the invention broadly concerns the changing of the fatty acid content of the bacterium. Specifically, applicant has discovered that bacteria transformed with the *fabB* gene, which results in the increase of percentage of unsaturated fatty acids in the cell membrane, causes the bacteria to have two unexpected properties. The first is that when these transformants are stored at low temperatures "greater than -80°C, preferably about -20°C to about 4°C" they will have a greater survival rate when subsequently plated, versus the parent strain from which they are derived. [See page 10, lines 6-9, for definition of "low temperatures" and in particular, page 14, lines 16 and 17.] The

second is that these transformants also have an enhanced transformation efficiency (greater than 100 fold) versus the strain from which they are derived. See page 30, Example 10. The specification at page 14, lines 3-4 lists several genes considered equivalent to *fabB* in that their over-expression will result in the increase in the percentage of unsaturated fatty acid in the cell membrane, and hence the same properties of the *fabB* gene over-expressers described in the specification as filed. Other than genes which directly increase the percentage of unsaturated fatty acids in the cell membrane, the specification fails to teach how a bacterium will be modified to result in the properties claimed. Other than direct introduction of such genes on plasmids for over-production of the gene product, the specification fails to teach how to increase expression of such genes, especially those located on the bacterial chromosome. Also, alteration of the fatty acid content is not commensurate with the teachings of the specification. The terms "alteration," "changing" or "modified" may include decreases in fatty acid content, yet that is not what is shown to result in bacteria having the properties claimed and in fact may have the opposite effect intended. Given the lack of guidance or direction presented, the lack of other working examples, the state of the prior art regarding teachings of increased viability or transformation frequency following cold storage, and the unpredictability of generating other mutants having the characteristics as claimed, the specification fails to enable the invention for its scope.

The following claim is suggested as an allowable method. Although the prior art teaches introduction of the *fabB* gene into *E. coli*, as well as transformants resulting from such

introduction, it does not teach methods for increasing the viability or transformation ability of these cells by introducing this gene. Support for the claim language is found at pages 50-54. Dependent claims may be drafted which specify the gene introduced or the bacteria species used, or further define the fatty acid content or temperature range.

A method for enhancing the viability during, or the enhancing the transformation ability following, storage of a bacterium at temperature ranges from about 4°C to about -80°C, said method comprising:

- a) introducing by transformation into an isolated bacterium, one or more genes encoding gene products which increase the amount of unsaturated fatty acids as a percentage of total fatty acids present in the cell membrane, and
- b) isolating transformants of a), wherein these transformants will have enhanced viability during, or enhanced transformation ability following, storage at temperature ranges from about 4°C to about -80°C when compared to the untransformed isolate bacteria of a).

It is noted that the specification at pages 16-17, Example 1, teaches that mutant strains which have increased viability properties have been generated by a different method from that in which the bacteria are modified by the introduction of exogenous nucleic acids. This method involves the cycling of cells through growth and storage at -20°C such that surviving cells having the desired properties are obtained. It is unclear what genetic properties such cells have that allow their increased survival, particularly for the cells designated SB3499B. Example 16 at page 51 indicates that these cells produced by this method also have increased levels of unsaturated fatty acids, but it is unclear how this occurs. Such mutants are uncharacterized genetically and, absent

evidence to the contrary, are unrelated to the transformants of the specification as described. Applicant is advised that if claims to this method are submitted, they will be considered to be drawn to an independent and distinct invention, unrelated to transformation methods, and will be subject to a restriction requirement. The current claims are interpreted to involve direct alteration of the bacteria by genetic means to effect a change the content of the unsaturated fatty acids, rather than selection processes that screen for mutants that survive storage at low temperatures.

Claims 1, 5-7, 9, 15, 19-21, 23, 32, 40 and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 1, it is unclear what the comprises the terms "modifying" and "altered" as they apply to the fatty acid content. The claim appears incomplete. Is the bacteria treated with a chemical to increase or decrease the fatty acid content, is the bacteria cultured in some manner, or is it genetically modified in some manner? Which fatty acids are so modified or altered? Also, the transformation efficiency is not enhanced during storage, but rather is demonstrated enhanced after storage. See also claims 15 and 32 in this regard.

Regarding claims 5-7 and 19-21, the term "unsaturated fatty acid genes" is vague and indefinite. The genes do not encode unsaturated fatty acids, but rather encode genes involved in the biosynthesis of unsaturated fatty acids.

Regarding claims 9, 23 and 40, the term is *Escherichia*, not *Escherchia*.

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Regarding claim 44, what "content" is unsaturated?

If applicant desires priority under 35 U.S.C. §120 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

The oath filed on 25 July 1997 in the parent application (of which the instant application is a Continuation filed under 35 U.S.C. §120) indicates on the first page that "the specification is attached hereto unless the following box is checked...". The box is not checked, so the oath refers to a specification which would be "attached hereto." This would be incorrect. A corrected oath is needed. Also, the oath does not claim benefit of the two provisional applications 60/014,330 and 60/025,838 as found in the first line of the specification.

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Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Art Unit 1636 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number for Art Unit 1636 is (703) 308-4242 or 305-3014.

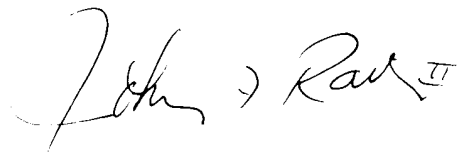
Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. F. Railey, whose telephone number is (703) 308-0281. The examiner can normally be reached on Monday-Thursday, and alternate Fridays, from 8:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, George Elliott, can be reached at (703) 308-4003. The fax phone number for informal transmissions to the examiner is (703) 305-7939.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

11 April 1999

**JOHNNY F. RAILEY II, PH.D.
PRIMARY EXAMINER
TECHNOLOGY CENTER 1600**

A handwritten signature in cursive script, appearing to read "John F. Railey II", is written over the printed name and title.